Page 4 of 18

Docket No.: 397272000401

Amendment to the Claims:

Please amend the claims as follows.

This listing of claims will replace all prior versions, and listing, of claims in the application:

Listing of Claims:

Claim 1 (original): A method for stable transduction of primary cells of the hematopoietic system and/or hematopoietic stem cells comprising contacting the surface of said cells with both a lentiviral vector and at least one molecule which binds said cell surface

wherein said contacting occurs in vitro or ex vivo and wherein greater than about 90% of the cells are stably transduced by after about 14 days.

Claim 2 (currently amended): The method of claim 1 <u>further comprising continuous</u>

<u>contacting wherein said contacting</u> the <u>primary cells or hematopoietic stem</u> cells <u>in vitro or ex vivo</u>

with <u>the a lentiviral vector after the occurs before contacting of the primary cells with <u>the lentiviral</u>

<u>vector and the at least one cell surface binding molecule.</u></u>

Claim 3 (currently amended): The method of claim 1 <u>further comprising continuous</u>

<u>contacting wherein said contacting</u> the <u>primary cells or hematopoietic stem</u> cells <u>in vitro or ex vivo</u>

with <u>the at least one cell surface binding molecule after the contacting of the</u> a lentiviral vector <u>and</u>

eccurs simultaneously with contacting the cells with at least one cell surface binding molecule.

Claim 4 (currently amended): The method of claim 1 <u>further comprising continuous</u>

<u>contacting wherein said contacting</u> the <u>primary</u> cells <u>or hematopoietic stem cells *in vitro* or *ex vivo*with <u>the</u> a lentiviral vector <u>and the at least one cell surface binding molecule after the initial contact</u>

<u>of the lentivirus vector and occurs after contacting</u> the <u>cells with</u> at least one cell surface binding

molecule.</u>

Claim 5 (original): The method of claim 1 where said contacting with a lentiviral vector occurs more than once.

Page 5 of 18

Docket No.: 397272000401

Claim 6 (currently amended): The method of claim 1 wherein said lentiviral vector is derived from HIV [[HIV-1]].

Claim 7 (currently amended): The method of claim 1 wherein said cell surface binding molecule is an antibody, an antigen binding fragment, a ligand or a cell surface molecule.

Claim 8 (original): The method of claim 1 wherein said lentiviral vector comprises at least one cis-acting nucleotide sequence derived from the gag, pol, env, vif, vpr, vpu, tat or rev genes.

Claim 9 (currently amended): The method of claim 8 wherein said <u>cis-acting nucleotide</u> sequence is not expressed or is a fragment or a mutant of the gag, pol, env, vif, vpr, vpu, tat or rev genes.

Claim 10 (currently amended): The method of Claim 1 wherein said lentiviral vector is derived from <u>HIV-1 or HIV-2</u>.

Claim 11 (original): The method of claim 1 wherein said lentiviral vector is a pseudotyped vector.

Claim 12 (currently amended): The method of claim 11 wherein said pseudotyped vector comprises contains the vesicular stomatitis virus G envelope protein.

Claim 13 (original): The method of claim 1 wherein said lentiviral vector is a chimeric vector comprising <u>HIV sequences</u>, wherein optionally the <u>HIV sequences</u> comprise <u>HIV-1</u> and <u>HIV-2</u> sequences.

Claim 14 (original): The method of claim 1 wherein said hematopoietic cell is a CD4 positive cell.

Page 6 of 18

Docket No.: 397272000401

Claim 15 (currently amended): The method of claim 1 wherein said <u>primary cell of the</u> hematopoietic <u>system or hematopoietic stem</u> cell is a lymphocyte.

Claim 16 (currently amended): The method of claim 1 [[15]] wherein the primary cell of the hematopoietic system or hematopoietic stem cell said lymphocyte is a CD4 or CD8 positive cell.

Claim 17 (currently amended): The method of claim 1 wherein said <u>primary cell of the</u> hematopoietic <u>system or hematopoietic stem</u> cell is a CD34 positive cell.

Claim 18 (currently amended): The method of claim 1 17 wherein said at least one cell surface binding molecule comprises a molecule selected from the group consisting of an FLT-3 ligand; a TPO ligand; a and Kit ligand; or antibodies that have are the functional analoge same cell surface binding specificity as FLT-3, TPO, or Kit ligand; CD3 ligand; a CD28 ligand; a CD25 ligand; a CD59 ligand; and, antibodies that have are the same cell surface binding specificity of CD3, CD25, CD28, CD69 or CD71 ligand.

Claim 19 (currently amended): The method of claim 1 wherein said at least one cell surface binding molecule comprises a molecule selected from the group consisting of FLT-3 ligand, TPO ligand and Kit ligand or polypeptides or other binding molecules antibodies that have are the same cell surface binding specificity as functional analogs FLT-3 ligand, TPO ligand, or Kit ligand

Claim 20 (currently amended): The method of <u>claim 1</u> any one of claims 1-12 wherein the said <u>primary</u> cell <u>or hematopoietic stem cell</u> is a dendritic cell or a cell capable of differentiating into a dendritic cell.

Claim 21 (currently amended): The method of claim 1 20 wherein said at least one cell surface binding molecule is selected from the group consisting of compositions comprising CD34.

CD3, CD28, GM-CSF, IL-4, and TNF-alpha; GM-CSF, and interferon-alpha; and or antibodies or

Page 7 of 18

Docket No.: 397272000401

other binding molecules that have the same ere functional analogs cell surface binding specificity as CD34, CD3, CD28, GM-CSF, IL-4, and TNF-alpha; GM-CSF or interferon-alpha.

Claim 22 (currently amended): The method of claim 14 wherein said at least one cell surface binding molecule is selected from the group consisting of CD3 antibodies and cell surface binding fragments thereof, CD28 antibodies and cell surface binding fragments thereof, and combinations of said antibodies and cell surface binding fragments thereof, and binding molecules that have the same cell surface binding specificities as the antibodies.

and optionally at least two of the cell surface binding molecules are immobilized on a bead or a surface.

Claim 23 (currently amended): The method of claim 22 wherein said at least one cell surface binding molecule comprises a combination of CD3 and CD28 antibodies immobilized on a bead or a surface, wherein optionally the bead or surface comprises coated beads.

Claim 24 (currently amended): The method of claim 1 [[3]] culturing the <u>primary</u> cells <u>or</u> <u>hematopoietic stem cells</u> under conditions conducive to growth and/or proliferation.

Claim 25 (original): The method of claim 24 wherein said conditions comprise further incubation with a cell surface binding molecule or a cytokine.

Claim 26 (original): The method of claim 25 wherein said cytokine is interleukin-2.

Claim 27 (original): The method of claim 24 wherein said culturing is for about seven days.

Claim 28 (original): The method of claim 24 wherein said culturing is for about 14 days.

Claim 29 (currently amended): The method of claim 1 [[3]] wherein said contacting the primary cells or hematopoietic stem cells with a lentiviral vector is for about 24 hours and is optionally repeated at least once.

Application No.: 10/664,331

Page 8 of 18

Claim 30 (original): The method of claim 1 wherein the lentiviral vector is present at an MOI of less than 500.

Claim 31 (original): A method to introduce genetic material into a living subject comprising introduction of a cell transduced by the method of claim 1.

Claim 32 (currently amended): The method of claim <u>31</u> [[3]] further comprising culturing the cells under conditions conducive to growth and/or proliferation.

Claim 33 (original): The method of claim 1 wherein said contacting occurs ex vivo.

Claim 34 (new): A method for stable transduction of primary cells of the hematopoietic system and/or hematopoietic stem cells comprising

- (a) isolating from an individual a primary cell of the hematopoietic system and/or a hematopoietic stem cell; and
- (b) contacting the primary cell or hematopoietic stem cell simultaneously in vitro or ex vivo with a lentiviral vector and the at least one cell surface binding molecule

wherein greater than 75% of the primary cells or hematopoietic stem cells are stably transduced by about 14 days,

and optionally the cell surface binding molecule comprises a polypeptide, a lipid, a nucleic acid, a carbohydrate or an ion.

Claim 35 (new): The method of claim 34 further comprising continuous contacting the primary cells or hematopoietic stem cells *in vitro* or *ex vivo* with the a lentiviral vector after the simultaneous contacting of the primary cells with the lentiviral vector and the at least one cell surface binding molecule.

Claim 36 (new): The method of claim 34 further comprising continuous contacting the primary cells or hematopoietic stem cells in vitro or ex vivo with the at least one cell surface binding

Application No.: 10/664,331

. Page 9 of 18

molecule after the simultaneous contacting of the a lentiviral vector and the at least one cell surface binding molecule.

Claim 37 (new): The method of claim 34 further comprising continuous contacting the primary cells or hematopoietic stem cells *in vitro* or *ex vivo* with the a lentiviral vector and the at least one cell surface binding molecule after the initial simultaneous contact of the lentivirus vector and the at least one cell surface binding molecule.

Claim 38 (new): The method of claim 34 where said contacting with a lentiviral vector occurs more than once.

Claim 39 (new): The method of claim 34 wherein said cells are human primary cells of the hematopoietic system and/or human hematopoietic stem cells.

Claim 40 (new): The method of claim 34 wherein said cell surface binding molecule is an antibody, an antigen binding fragment, a ligand or a cell surface molecule.

Claim 41 (new): The method of claim 34 wherein said lentiviral vector comprises at least one cis-acting nucleotide sequence derived from the gag, pol, env, vif, vpr, vpu, tat or rev genes.

Claim 42 (new): The method of claim 41, wherein said cis-acting nucleotide sequence is not expressed or is a fragment or a mutant of the gag, pol, env, vif, vpr, vpu, tat or rev genes.

Claim 43 (new): The method of claim 34 wherein said lentiviral vector is an HIV-derived vector.

Claim 44 (new): The method of claim 34 wherein said lentiviral vector is a pseudotyped vector.

Page 10 of 18

Docket No.: 397272000401

Claim 45 (new): The method of claim 44 wherein said pseudotyped vector contains the vesicular stomatitis virus G envelope protein.

Claim 46 (new): The method of claim 34 wherein said primary cell or hematopoietic stem cell is a primary human cell or a human hematopoietic stem cell.

Claim 47 (new): The method of claim 34 wherein said primary cell of the hematopoietic system or hematopoietic stem cell is a CD4 positive cell.

Claim 48 (new): The method of claim 34 wherein said primary cell of the hematopoietic system or hematopoietic stem cell is a lymphocyte.

Claim 49 (new): The method of claim 48 wherein said lymphocyte is a CD4 or CD8 positive cell.

Claim 50 (new): The method of claim 34 wherein said primary cell of the hematopoietic system or hematopoietic stem cell is a CD34 positive cell.

Claim 51 (new): The method of claim 34 wherein said primary cell of the hematopoietic system is a human hematopoietic stem cell.

Claim 52 (new): The method of claim 34 wherein said at least one cell surface binding molecule comprises a molecule selected from the group consisting of FLT-3 ligand; a TPO ligand; a Kit ligand; an antibody that has the same cell surface binding specificity as FLT-3, TPO, or Kit ligand; a CD3 ligand; a CD28 ligand; a CD25 ligand; a CD71 ligand; a CD69 ligand; and, an antibody that has the same cell surface binding specificity of CD3, CD25, CD28, CD69 or CD71 ligand.

Application No.: 10/664,331

Page 11 of 18

Claim 53 (new): The method of claim 34 wherein said at least one cell surface binding molecule comprises a molecule selected from the group consisting of FLT-3 ligand, TPO ligand and Kit ligand or polypeptides or other binding molecules that have the same cell surface binding specificity as FLT-3 ligand, TPO ligand, or Kit ligand.

Claim 54 (new): The method of claim 34 wherein the said primary cell or hematopoietic stem cell is a dendritic cell or a cell capable of differentiating into a dendritic cell.

Claim 55 (new): The method of claim 34 wherein said at least one cell surface binding molecule is selected from the group of compositions comprising a CD34, a CD3, a CD28, a GM-CSF, an IL-4, a TNF-alpha; a GM-CSF; an interferon-alpha; and an antibody or other binding molecule that has the same cell surface binding specificity as CD34, CD3, CD28, GM-CSF, IL-4, and TNF-alpha, GM-CSF or interferon-alpha.

Claim 56 (new): The method of claim 34 wherein said at least one cell surface binding molecule is selected from the group consisting of CD3 antibodies and cell surface binding fragments thereof, CD28 antibodies and cell surface binding fragments thereof, combinations of said antibodies and cell surface binding fragments thereof, and binding molecules that have the same cell surface binding specificities as the antibodies,

and optionally at least two of the cell surface binding molecules are immobilized on a bead or a surface.

Claim 57 (new): The method of claim 56 wherein said at least one cell surface binding molecule comprises a combination of CD3 and CD28 antibodies immobilized on coated beads.

Claim 58 (new): The method of claim 34 further comprising culturing the primary cells or hematopoietic stem cells under conditions conducive to growth and/or proliferation.

Application No.: 10/664,331

Page 12 of 18

Claim 59 (new): The method of claim 58 wherein said conditions comprise further incubation with a cell surface binding molecule or a cytokine.

Claim 60 (new): The method of claim 59 wherein said cytokine is interleukin-2.

Claim 61 (new): The method of claim 58 wherein said culturing is for about seven days.

Claim 62 (new): The method of claim 58 wherein said culturing is for about 14 days.

Claim 63 (new): The method of claim 34 wherein said contacting the primary cells or hematopoietic stem cells with a lentiviral vector is for about 24 hours and is optionally repeated at least once.

Claim 64 (new): The method of claim 34 wherein the lentiviral vector is present at an MOI of less than about 500.

Claim 65 (new): A method to introduce a genetic material into a cell comprising ex vivo introduction of the cell transduced by the method of claim 1 into a tissue, an organ, a blastocyst or an embryonic stem cell.

Claim 66 (new): The method of claim 34 wherein said contacting occurs ex vivo.

Claim 67 (new): The method of claim 34 wherein said lentiviral vector is derived from a human immunodeficiency virus (HTV), wherein optionally the HIV is HIV-1 or HIV-2.

Claim 68 (new): The method of claim 34 wherein said lentiviral vector is a chimeric vector comprising HIV-1 and HIV-2 sequences.

Application No.: 10/664,331

Page 13 of 18

Claim 69 (new): The method of claim 1 or claim 34, wherein greater than 80%, 85%, 89%, 90%, 91%, 92%, 93%, 94% or 95% of the cells are stably transduced after about 14 days.

Claim 70 (new): The method of claim 34 wherein the individual is infected with a human immunodeficiency virus (HIV), wherein optionally the HIV is HIV-1 or HIV-2.

Claim 71 (new): The method of claim 1 or claim 34, wherein the primary cells or hematopoietic stem cells isolated from the HIV-infected individual are pre-stimulated with at least one cell surface binding molecule, and optionally the primary cells or hematopoietic stem cells are pre-stimulated with the at least one cell surface binding molecule within twenty four (24) hours prior to simultaneously contacting the primary cells or hematopoietic stem cells in vitro or ex vivo with the lentiviral vector and the at least one cell surface binding molecule.

Claim 72 (new): A method for stable transduction of a primary cell of the hematopoietic system and/or a hematopoietic stem cell isolated from an HTV-infected individual, comprising the steps of:

- (a) isolating from the HIV-infected individual primary cells of the hematopoietic system cells or hematopoietic stem cells;
- (b) pre-stimulating the primary cells or hematopoietic stem cells with at least one cell surface binding molecule,

wherein optionally the primary cells or hematopoietic stem cells are pre-stimulated with at least one cell surface binding molecule within twenty four (24) hours prior to step (c), or optionally the pre-stimulation with at least one cell surface binding molecule is for 12 to 96 hours; and

(b) contacting simultaneously in vitro or ex vivo the hematopoietic system cells or hematopoietic stem cells with a lentiviral vector and at least one cell surface binding molecule,

wherein after the contacting greater than 75% of the cells are stably transduced by about 14 days, and optionally the cell surface binding molecule comprises a polypeptide, a lipid, a nucleic acid, a carbohydrate or an ion.

Page 14 of 18

Docket No.: 397272000401

Claim 73 (new): The method of claim 72, wherein greater than 80%, 85%, 89%, 90%, 91%, 92%, 93%, 94% or 95% of the cells are stably transduced by 14 days.

Claim 74 (new): A pharmaceutical composition comprising a primary cell of the hematopoietic system or hematopoietic stem cell transduced by the method of claim 1.

Claim 75 (new): The pharmaceutical composition of claim 74, wherein the pharmaceutical composition is formulated for the treatment or prevention of a disease or a condition in a subject.

Claim 76 (new): The pharmaceutical composition of claim 74, wherein the pharmaceutical composition is formulated for the treatment or prevention of a viral infection in a subject.

Claim 77 (new): The pharmaceutical composition of claim 74, wherein the pharmaceutical composition is formulated for the treatment or prevention of an HIV infection in a subject.

Claim 78 (new): The pharmaceutical composition of claim 74, wherein the pharmaceutical composition is formulated for the treatment or prevention of a tumor or a cancer, wherein optionally the tumor or cancer is breast cancer.

Claim 79 (new): The pharmaceutical composition of claim 74, wherein pharmaceutical composition, wherein the pharmaceutical composition is formulated for the treatment or prevention of a tumor, wherein optionally the tumor is a tumor of endothelial cells.

Claim 80 (new): The pharmaceutical composition of claim 75, wherein the subject is a human.

Claim 81 (new): The pharmaceutical composition of claim 76, wherein the subject is infected with human immunodeficiency virus (HIV), wherein optionally the HIV is HIV-1 or HIV-2.

Page 15 of 18

Docket No.: 397272000401

Claim 82 (new): The pharmaceutical composition of claim 74, wherein the pharmaceutical composition is formulated for use ex vivo.